

Computational Study on Nature of Transition Structure for Oxygen Transfer from Dioxirane and Carbonyloxide

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ABSTRACT: The relative reactivity of a series of nucleophiles that includes ethylene, sulfides, sulfoxides, amines, and phosphines toward dioxirane, dimethyldioxirane, carbonyloxide and dimethylcarbonyloxide has been examined at the MP4/6-31G*//MP2/6-31G*, QCISD(T)/6-31G*//MP2/6-31G*, and B3-LYP/6-31G* levels of theory. The barriers for the oxidations with dimethyldioxirane are higher (up to 2.5 kcal/mol for the oxidation of H₂S) than those for the oxidations with the parent dioxirane. The oxidation barriers for dioxirane are larger than those for the oxidations with peroxyformic acid, except the barriers for the oxidation of sulfoxides. The reactivity of dimethylsulfide toward dimethyldioxirane was found to be comparable to that of dimethylsulfoxide both in the gas phase and in solution (chloroform). The classical gas phase barrier for the oxidation of trimethylamine to trimethylamine oxide was higher (6.3 kcal/mol at the MP4//MP2/6-31G* level) than that for oxygen atom transfer to trimethylphosphine. When the transition states were examined by self-consistent reaction field (SCRF) methods, the predicted barriers for the oxidation of amines and phosphines were found to be in good agreement with experiment. The general trend in reactivity for oxidation by dioxirane was R₂S ≈ R₂SO, R₃P > R₃N in the gas phase, and R₂S ≈ R₂SO, R₃N ≈ R₃P (R =

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Me) in solution. The oxidation barriers calculated using the B3-LYP functional were lower than those computed at the MP4 and QCISD(T) levels. © 1998 John Wiley & Sons, Inc. J Comput Chem 19: 1353–1369, 1998

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Introduction

The distinction between chemical descriptors such as electrophiles and nucleophiles has become more difficult to define. Relative nucleophilic character is typically assigned to those reagents that readily donate an electron pair to a reagent that has been deemed electrophilic in nature. When one nucleophile is considered to be more reactive than another, the relative reactivity is typically that measured in solution. Among those properties that influence nucleophilicity are the degree of solvation of the nucleophile, its effective size and electronegativity, and the polarizability of the attacking atom. For example, third row elements are considered to be more nucleophilic than the second row counterparts and this increased nucleophilicity is often ascribed to their greater polarizability.¹

Despite the fact that peroxides contain an O—O bond with four lone pairs of electrons, they have been classified as electrophiles.² We have attempted to clarify this description by emphasizing the fact that a peroxide has a relatively weak bond that has an empty (electrophilic) σ^* orbital that decreases rapidly in energy upon O—O bond elongation induced by the attack of a nucleophile.^{3a} Dioxiranes are paradigm examples of electrophilic species. They are three-membered-ring, highly strained peroxides that serve as powerful oxidants in synthetic organic chemistry.⁴

The simplest dioxirane, H_2CO_2 , has only been observed as a fleeting intermediate in low temperature ozonolysis studies. Dioxirane was first predicted in a mechanistic study of the Criegee intermediate in ozonolysis in 1949.^{5a} Its structure has since been determined by microwave spectroscopy.^{5b, 6a} The majority of theoretical study on this class of compounds has been restricted to this unsubstituted parent peroxide.⁶ It was evident from early theoretical calculations^{6a} that this would be a relatively unstable compound, because it has several isomeric forms, including dioxymethylene,

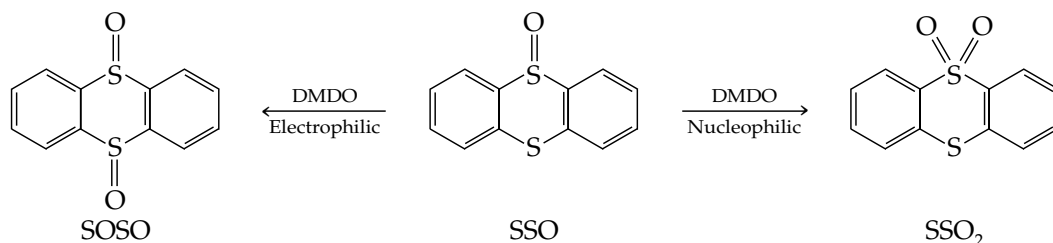
OCH_2O , which was predicted^{6b, c} to be only 15 kcal/mol higher in energy than dioxirane.

Dimethyldioxirane,⁴ however, is a powerful oxidant with unusual synthetic utility, than can be produced readily *in situ* by the reaction of acetone with caroate ($2 \text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$).⁷ Recent efforts to isolate dimethyldioxirane (DMDO) have proven successful and it is sufficiently stable to remain in solution for several days at room temperature.⁸ It can readily epoxidize alkenes, insert oxygen into carbon–hydrogen bonds, and it oxidizes nucleophiles such as amines, phosphines, and sulfides. Methyl(trifluoromethyl)dioxirane (TFDO)^{8a} was synthesized a few years later and it was demonstrated that electron-withdrawing groups can markedly enhance the oxygen donor propensity of these cyclic peroxides.^{2a} Indeed, TFDO is about 100 times more reactive than DMDO and it is capable of oxidizing saturated hydrocarbons to their alcohols at relatively low temperatures.⁹ The sterically encumbered dimesityldioxirane is stable in the solid phase, but in solution it slowly rearranges to its ester.¹⁰ Difluorodioxirane, F_2CO_2 , is the only simple, known substituted dioxirane that can be readily isolated as a pure substance and is thermally stable. It exists in the gaseous state at room temperature. There have been several theoretical¹¹ and experimental⁴ studies on this dioxirane.

The simplest carbonyl oxide, CH_2OO , is another potential oxygen donor that was part of the Criegee ensemble of high-energy intermediates in the ozonolysis mechanism.^{5a} There are several studies on the cyclization of carbonyl oxides to dioxirane.¹² It was established that the cyclization of carbonyl oxide to dioxirane is not competitive with the cycloaddition of carbonyloxides to another carbonyl compound to give an ozonide.¹³ Dioxiranes are more stable than carbonyloxides, and the barriers for their interconversion are higher than the barriers for epoxidation of alkenes.³

The oxidation of sulfides to sulfoxides and to sulfones by dimethyldioxirane (DMDO) has attracted the interest of both theoretical and experimental chemists. Adam and coworkers^{13a} studied

the following reaction:



In these experiments, the oxidation of 5-thianthrene oxide to 5,10-dioxide (SOSO) was favored over the 5,5-dioxide (SSO₂). Later, the oxidation of SSO was used as a mechanistic probe to determine the electronic character of the oxidants.^{13b} McDouall studied the oxidation of the unsubstituted sulfide by *ab initio* calculations.¹⁴ These results suggested SSO₂ as the major product. In a recent study,^{13c} Adam and Golash confirmed the electrophilic character of DMDO and suggested that SSO is a reliable mechanistic probe to examine the electronic character of oxygen transfer.

Our goal is to study the barrier heights for the oxidation of sulfides and sulfoxides by the parent dioxirane and DMDO using *ab initio* molecular orbital methods, such as MP2, MP4, B3-LYP, and QCISD(T) levels of theory. Calculated solvent effects are used to model the experimental conditions.

Theoretical studies have also been carried out on the oxidation of amines and phosphines by peroxyformic acid.^{3a} However, little theoretical attention has been paid to the oxidation of amines and phosphines by dioxiranes. A second goal in this study, is to investigate the oxidations of amines and phosphines by the parent dioxirane and DMDO in the gas and condensed phase. We are also interested in studying the chemical reactivity of the parent carbonyl oxide and dimethylcarbonyl oxide (DMCO) toward amines, phosphines, sulfides, and sulfoxides in the gas phase. The condensed phase investigation is limited to oxidation by the parent carbonyl oxides.

Method of Calculations

Molecular orbital calculations were carried out using the Gaussian-94 program system^{15a} utilizing gradient geometry optimization.^{15b} The geometries

of nucleophiles [H₂S, H₂SO, NH₃, PH₃, (CH₃)₂S, (CH₃)₂SO, (CH₃)₃N, (CH₃)₃P, and C₂H₄], and the transition structures were fully optimized without geometry constraints with the 6-31G* basis set using second-order Møller–Plesset perturbation theory with frozen core orbitals (denoted further as MP2/6-31G*). Single-point calculations were carried out with MP2/6-31G*-optimized geometry using MP4 and QCISD(T) levels of theory with frozen core orbitals. Vibrational frequencies were calculated at the MP2/6-31G* level to verify the nature of these transition states. Total energies and dipole moments for the reactants and transition states of the oxidation reactions are listed in Tables IS and IIS (Supplementary Material).

Structures for the reactions involving dioxiranes were also optimized using the B3-LYP/6-31G* level of density functional theory, with vibrational frequencies calculated at the same level. Because some of the transition structures have rather long bonds, stability calculations were carried out at both the HF/6-31G* and B3-LYP/6-31G* levels. Eigenvalues of the RHF stability matrix for the unstable and stable wave functions, values of S², and the energies for the stable solutions are listed in Table IIIS (Supplementary Material). The effects of solvation were estimated with Tomasi's polarized continuum model (PCM)^{16a,b} at the MP2/6-31G* level using the gas phase MP2/6-31G*-optimized geometries. For the PCM model the sphere radii assigned to each atom were dependent on the atom type and basis set.^{16c} The level of theory required to describe adequately the ground state scission of the oxygen–oxygen bond in peroxides has been the subject of considerable debate.^{3,17} We have found that treatment of dynamic correlation at the MP2 level of theory is adequate for oxygen atom transfer from hydroperoxides and peroxyacids.³

The barrier heights for the oxidations of various nucleophiles with dioxirane are presented in Table I and for carbonyl oxide in Table II; the corresponding energies of reactions are shown in Table III. For some of the transition states, the RHF wave functions show a UHF instability (Table IIIS). When UHF and UMPn calculations are carried out on these structures, there is a significant change in energy, as expected from the sizable spin contamination. It has been shown previously by Chen and Schlegel¹⁸ that restricted and unrestricted QCI and coupled cluster calculations can treat moderately stretched bonds quite well. For bond elongations up to 60–80%, the restricted and unrestricted QCI (or CC) energies are quite similar and the spin contamination is less than 0.2 for the unrestricted QCI (or CC) wave functions. The bonds in the transition states considered in the present study are elongated by less than 50% and, for the worst case (PH₃ + DMDO), the difference between the RQCISD(T) and UQCISD(T) energies is only 4 kcal/mol. This indicates that the RQCISD(T) calculations are satisfactory for these transition states.

The geometries of dioxirane optimized at the MP2/6-31G* and QCISD/6-31G* levels of theory are close to each other, as well as to the experimental data^{5c} (Table IV). These data combined with our computational results on similar oxida-

tions of amines, sulfides, and phosphines with peroxyxynitrous acid^{3d} allows us to conclude that the MP2 method is capable of providing reliable geometrical data. The energy difference between cyclic dioxirane and the 2π state, an open-chain structure that corresponds to methylenebis(oxy) (“dioxymethane”), is 11.6 kcal/mol at the QCISD(T)/6-31G*//MP2/6-31G* level.^{3b} This energy difference is close to values of 12.3 and 11.1 kcal/mol calculated at the QCISD(T)/6-31G*//QCISD/6-31G* and CASPT2 levels of theory, respectively.^{3e,6e} The energy difference between the parent dioxirane and carbonyl oxide computed at the QCISD(T)/6-31G*//MP2/6-31G* level (Table V) agrees with the data of the CCSD(T)/TZ2P calculations.^{12b} Therefore, we can expect that the energetics for oxidations with dioxirane and carbonyl oxide calculated using the QCISD(T)/6-31G*//MP2/6-31G* level of theory is reliable.

Results and Discussion

DIOXIRANE AND CARBONYLOXIDE

The reactions of substituted dioxiranes and carbonyl oxides with various nucleophiles result in

TABLE I. Barriers^a for Oxidations of Various Nucleophiles by Dioxirane and Dimethyldioxirane (DMDO).

	Gas phase				Solution ^b		$\langle \mu \rangle^c$
	MP2	MP4	QCISD(T)	B3-LYP	CHCl ₃	CH ₃ OH	
H ₂ S + dioxirane	27.3	24.2	24.9	19.4	13.4	10.9	11.6
H ₂ S + DMDO	30.1	26.7	27.5	24.2			14.3
Me ₂ S + DMDO	12.4	9.4		10.0	2.2		8.7
H ₂ SO + dioxirane	12.3	4.1	15.0	10.7	11.8	−3.5 ^d	7.2
H ₂ SO + DMDO	14.6	6.1	16.9	14.2			5.9
Me ₂ SO + DMDO	9.3	6.2		9.6	−3.4 ^d		6.0
NH ₃ + dioxirane	26.7	22.3	22.2	15.8	7.7	4.6	12.6
NH ₃ + DMDO	28.6	23.9	23.8	19.7			12.8
Me ₃ N + DMDO	10.7	6.3		10.8	2.2		8.6
PH ₃ + dioxirane	7.1	7.9	9.5	7.4	5.5	5.5	5.8
PH ₃ + DMDO	8.8	9.6	11.6 ^e	11.5			12.0
Me ₃ P + DMDO	0.5	1.0		3.2	0.8		3.2

^aIn kilocalories per mole, with the 6-31G* basis set; MP2, MP4, and QCI at the MP2-optimized geometry and B3-LYP at the B3-LYP-optimized geometry.
^bUsing Tomasi's polarized continuum model at the MP2/6-31G* level.
^cThe transition structures dipole moments (in Debye) were calculated at the HF/6-31G* level of theory.
^dThe barriers given with respect to the isolated reactants can be negative although the central barriers relative to the prereaction complexes are, of course, positive.
^eThe UQCISD(T) barrier is 15.6 kcal/mol.

TABLE II.
Barriers^a for Oxidations of Various Nucleophiles by Carbonyloxide and Dimethylcarbonyloxide (DMCO).

	Gas phase			Solution ^b	
	MP2	MP4	QCISD(T)	CHCl ₃	CH ₃ OH
H ₂ S + carbonyloxide	18.4	16.5	14.8	15.2	14.63
H ₂ S + DMCO	17.5	15.0	14.6		
H ₂ SO + carbonyloxide	7.6	0.5	5.2	−6.9 ^c	
H ₂ SO + DMCO	7.2	−0.5 ^c	5.7		
NH ₃ + carbonyloxide	18.8	16.6	14.2	14.9	14.1
NH ₃ + DMCO	18.7	15.7	14.8		
PH ₃ + carbonyloxide	11.7	11.1	9.2	8.8	1.9
PH ₃ + DMCO	8.6	7.8	7.6		
C ₂ H ₄ + carbonyloxide	14.8	13.9		11.6	11.1
C ₂ H ₄ + DMCO	12.9				

^aIn kilocalories per mole, with the 6-31G* basis set; MP2, MP4, and QCI at the MP2-optimized geometry and B3-LYP at the B3-LYP-optimized geometry.

^bUsing Tomasi's polarized continuum model at the MP2/6-31G* level.

^cSee footnote d in Table I.

TABLE III.
Reaction Energies^a for Oxidation of Various Nucleophiles by Dioxirane, Dimethyldioxirane (DMDO), Carbonyloxide, and Dimethylcarbonyloxide (DMCO).

	MP2	MP4	QCISD(T)	B3-LYP
H ₂ S + dioxirane	−18.0	−11.1	−16.5	−17.5
H ₂ S + DMDO	−14.3	−7.5	−12.9	−16.6
Me ₂ S + DMDO				−35.5
H ₂ S + carbonyloxide	−52.5	−40.3	−45.0	
H ₂ S + DMCO	−47.1	−35.4	−39.1	
H ₂ SO + dioxirane	−62.5	−64.3	−56.7	−54.6
H ₂ SO + DMDO	−58.7	−60.8	−53.1	−53.7
Me ₂ SO + DMDO				−61.1
H ₂ SO + carbonyloxide	−97.0	−93.5	−85.3	
H ₂ SO + DMCO	−91.6	−88.6		
NH ₃ + dioxirane	4.5	3.9	3.4	1.3
NH ₃ + DMDO	8.2	7.5	7.0	2.2
Me ₃ N + DMDO				−15.5
NH ₃ + carbonyloxide	−30.0	−25.3	−25.2	
NH ₃ + DMCO	−24.6	−20.4	−19.3	
PH ₃ + dioxirane	−71.3	−67.0	−65.6	−64.2
PH ₃ + DMDO	−67.6	−63.4	−62.0	−63.3
Me ₃ P + DMDO				−86.6
PH ₃ + carbonyloxide	−105.8	−96.2	−94.1	
PH ₃ + DMCO	−100.4	−91.3	−88.2	

^aIn kilocalories per mole, with the 6-31G* basis set; MP2, MP4, and QCI at the MP2-optimized geometry and B3-LYP at the B3-LYP-optimized geometry.

TABLE IV.
Geometries of Dioxirane and Bis(oxy)methylene (2π Ground State) Calculated at Various Computational Levels and Experimental Data^a

	MP2 / 6-31G* ^b	QCISD / 6-31G*	Exp. ^c
Dioxirane			
C—O	1.398	1.395	1.388
O—O	1.530	1.522	1.516
∠O—C—O	66.4	66.2	66.2
Bis(oxy)methylene $2\pi^1A_1$			
C—O	1.374	1.308	
O—O	2.459	2.366	
∠O—C—O	127.1°	129.4°	

^aBond distances are in angstroms, bond angles are in degrees.
^bMP2(full) calculations.
^cTaken from ref. 5c.

breaking the O—O bond in a manner that can involve a series of biradical states that can be designated 2π , 3π , and 4π .^{6b,c,e} In previous studies,^{3b} we found that the 2π biradical state for the parent dioxirane was the lowest singlet, but that only the 4π states were involved in oxygen transfer to nucleophiles having a lone pair of electrons or an alkene π -bond.

In this study, we examine the chemistry of dimethyldioxirane, methyl(trifluoromethyl)dioxirane, and difluorodioxirane. The first two reagents are the most commonly used forms of dioxirane in practical oxidation reactions; the difluoro species was chosen to probe the effect of very electronegative substituents. The relative energies of several selected substituted dioxiranes and carbonyloxides are summarized in Table V. Their corresponding optimized geometries are presented in Figure 1. Unsubstituted dioxirane lies ca.

30 kcal/mol lower than carbonyl oxide, and is separated from it by a barrier of ca. 50 kcal/mol.^{3b} Thus, the calculations indicate that dioxirane and carbonyl oxide react as separate and distinct species, in agreement with experiment.² Whereas dimethyl- and methyl-trifluoromethyl substitution have very little effect on energy of the isomerization of dioxirane into carbonyl oxide, difluoro substitution raises the energy of carbonyl oxide by ca. 20 kcal/mol.

OXIDATION OF SULFIDES AND SULFOXIDES WITH DIOXIRANE

One of the current mechanistic questions relevant to this study is the relative nucleophilicity of a sulfide versus its sulfoxide and the use of these functional groups to assess the electronic nature of oxygen-transfer reagents. In these studies it was recognized that the preferential complexation of the oxidizing agent with either the sulfur or sulfoxide moiety could alter the chemoselectivity of competitive oxidation. The oxidation of sulfides shows no clear dependence of rates on solvent dielectric constant but rather upon specific interactions between solvent and solute.¹³ Under typical laboratory conditions the oxidation of a sulfide can be stopped readily at the sulfoxide stage if desired [eq. (1)] and its sulfone is not formed unless additional oxidizing agent is added or more vigorous reaction conditions are introduced.

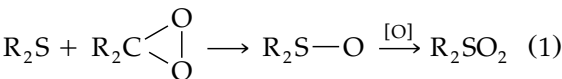


TABLE V.
Isomerization Energies for Dioxirane and Substituted Dioxiranes.^a

	Dioxirane → Carbonyl oxide
Dihydrogendioxirane	34.5 (28.5) ^{b,c}
Dimethyldioxirane	32.9
Methyl(trifluoromethyl)dioxirane	35.7
Difluorodioxirane	55.6 ^d

^aIn kilocalories per mole, at the MP2 / 6-31G* level.
^bQCISD(T) / 6-31G* // MP2 / 6-31G* value given in parentheses.
^cA value of 25.6 kcal / mol at the CCSD(T) / TZ2P level.^{12b}
^dA value of 47 kcal / mol at the CCSD(T) / cc-VTZ2P + f level.^{12c}

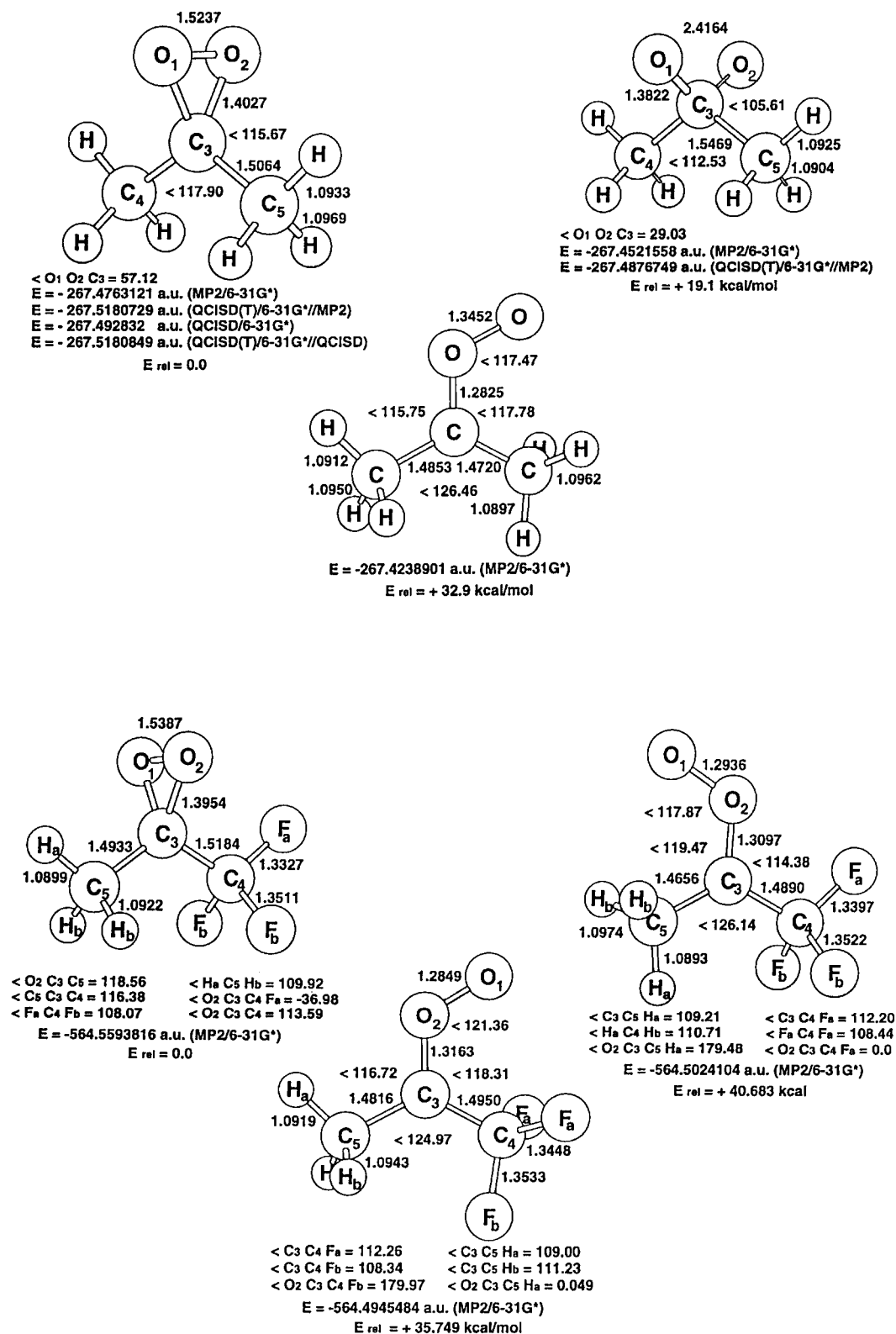


FIGURE 1. The geometry for dimethyldioxirane, its 2π biradical, dimethylcarbonyl oxide, difluorodioxirane, its 2π biradical, difluorocarbonyl oxide, methyl(trifluoromethyl)dioxirane and methyl(trifluoromethyl)carbonyloxide optimized at the MP2/6-31G* level of theory. The relative energies calculated at various levels of theory are given in Table V.

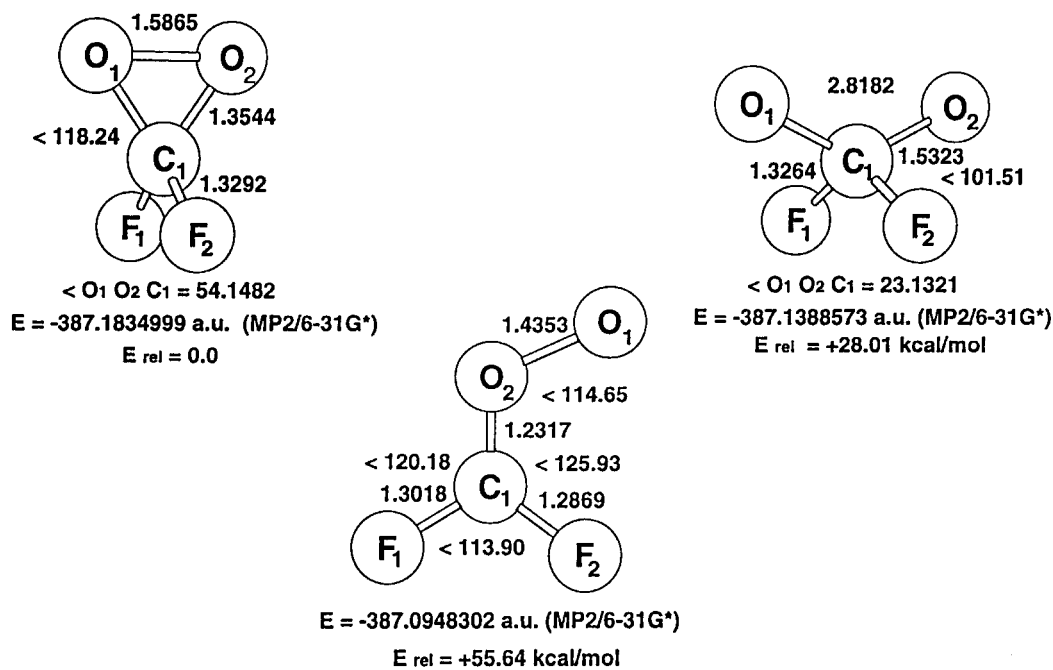


FIGURE 1. Continued.

The oxidations of H₂S and H₂SO by the parent dioxirane have been considered previously by McDouall¹⁴ at the MP2(full)/6-31G* level of theory. The current calculations using the frozen core approximation are included for a comparison with the B3-LYP/6-31G* calculations. These data can also be compared with the oxidation of sulfides and sulfoxides by peroxyformic acid.

Very similar transition state geometries (Fig. 2) are obtained for the oxidation of H₂S by dioxirane (TS-1), H₂S by dimethyldioxirane (TS-2), and Me₂S by dimethyldioxirane (TS-3). Oxidation proceeds by nucleophilic attack of the higher lying p_π sulfur lone pair of electrons on the O—O bond in an S_N2-like manner. The S—O and O—O bonds in TS-3 are 1.90 (1.99) Å and 1.97 (1.95) Å, respectively, at the MP2 (B3-LYP) level. The S—O—O angle of 169° is consistent with this type of nucleophilic displacement. The S—O and O—O bond lengths are quite comparable to those observed for peroxyformic acid oxidation of H₂S and Me₂S,^{3a} but are significantly different from those found for oxidation by carbonyl oxide (see subsequent text). The MP4//MP2/6-31G* barrier for TS-3 (9.4 kcal/mol; Table I) is 2.8 kcal/mol higher than that predicted for dimethylsulfoxide (DMSO) formation by the action of peroxyformic acid. This is a rather surprising trend because it has generally been assumed that relief of ring strain would make

dioxirane a more reactive oxygen donor than the simplest peroxyacid.

The transition structures (TS-4 and TS-5) for the dioxirane oxidation of the sulfoxides H₂SO and DMSO are also very similar to each other (Fig. 3). The transition structure for oxygen transfer from DMDO to DMSO has a nearly linear S—O—O bond angle as a consequence of steric repulsion due to the methyl groups. The oxidation of sulfoxides by dioxirane, carbonyl oxide, and peroxyformic acid³ are all characterized by rather large S—O—O angles. The attack by the sulfoxide sulfur on the O—O bond makes an effort to avoid the lone pair of electrons on sulfur. For the sulfides as well as for the sulfoxides, methyl substitution of the dioxirane has very little effect on the geometry, but methyl substitution of the nucleophile moves the transition state toward the reactants. For both the sulfide and the sulfoxide, methyl substitution on the dioxirane raises the barrier by 2–3 kcal/mol, but methyl substitution on the sulfur lowers the barrier ca. 17 kcal/mol for the sulfide and ca. 5 kcal/mol for the sulfoxide. A similar effect of methyl substitution on the nucleophile was seen in oxidations with peroxyformic acid.^{3a}

For the oxidation of H₂S by dioxirane, the gas phase barrier heights computed at the MP4 and QCISD(T) levels are in very good agreement with each other, and are ca. 3 kcal/mol lower than the

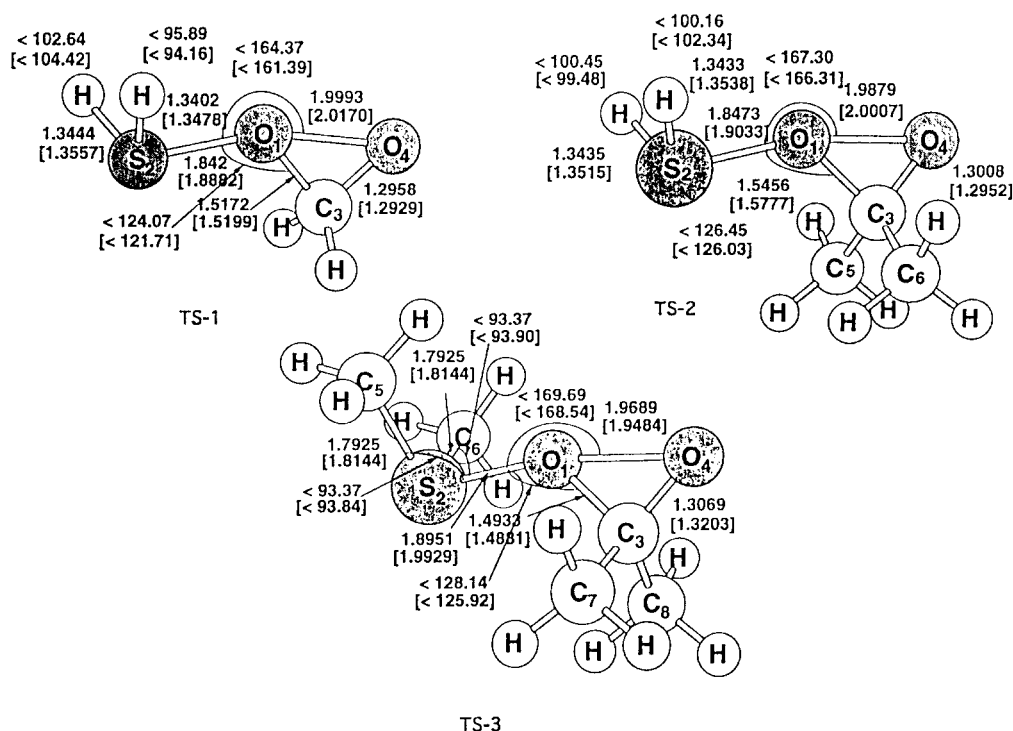


FIGURE 2. Transition structures for oxygen transfer from dioxirane and dimethyldioxirane to hydrogen sulfide and dimethylsulfide optimized at the MP2/6-31G* and B3-LYP/6-31G* (in square brackets) levels of theory.

MP2 values. For the oxidation of H_2SO , the large difference between the MP4 and QCISD(T) results can be traced to the RHF \rightarrow UHF instability of the RHF wave function (an eigenvalue of -0.125 of the stability matrix). The QCISD(T) approach gives a barrier about 10 kcal/mol higher than the MP4 barrier for the sulfoxide oxidations. It was shown previously¹⁸ that errors in the energy associated with the RHF \rightarrow UHF instability and spin contamination are much smaller with QCI and CC methods than with Møller–Plesset theory. Hence, the QCISD(T) barriers are more reliable than the MP4 barriers. The RB3-LYP calculations, which exhibit no wave function instability problems, lead to barrier heights 3–5 kcal/mol lower than the QCISD(T) values. However, the trends in the B3-LYP barriers agree very well with the QCISD(T) data (Table I).

A general comment regarding the use of H_2S and H_2SO as model substrates for sulfides and sulfoxides is in order. In earlier theoretical studies using H_2S and H_2SO it was assumed that theory gave the opposite trend to that noted in experiment. It is well established that, under the appropriate reaction conditions, a sulfide can be selectively oxidized to its sulfoxide without further oxidation. Thus, it is generally assumed that sulfides are much more “nucleophilic” than sulfox-

ides. However, seminal studies by Edwards and coworkers¹⁹ have shown that k_s/k_{so} varies from 3.3 in dioxane solvent to 900 in trifluoroethanol.²⁰ We have found that the intrinsic gas phase reactivities of a sulfide and its sulfoxide with peroxyformic acid are quite comparable, and that this reactivity ratio is an effect of preferred solvation.^{3a} The change in dipole moment in going from sulfide to sulfoxide is quite large and the TS is more solvated than the ground state. In contrast, the ground state of a sulfoxide is more highly solvated than its TS because the increase in dipole moment in the sulfone TS is minimal. These opposite effects conspire to control k_s/k_{so} if the proper choice of solvent is made. We now find the same effect for dioxirane oxidation as observed for peroxy acids. In protic solvents, nucleophilicity and basicity are not parallel. With Tomasi’s polarized continuum model for solvation,^{16a,b} the barriers for oxidation of the sulfides are lowered much more than for the sulfoxides. This is consistent with the large difference between the reactant and transition state dipole moments for the sulfide (ca. 10 D) compared with a much smaller difference for the sulfoxide (ca. 2.5 D) (Tables IS and IIS). A similar effect was found for oxidation by peroxyformic acid.^{3a} Thus, both appropriate substitution on the

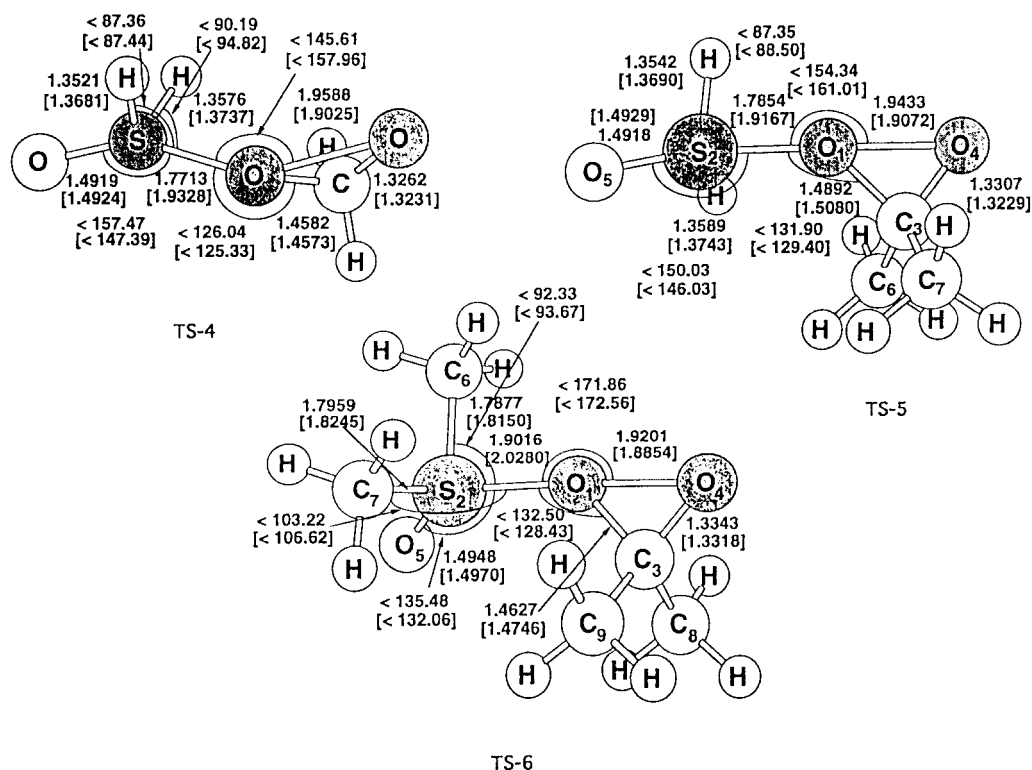


FIGURE 3. Transition structures for oxygen transfer from dioxirane and dimethyldioxirane to dihydrogen sulfoxide and dimethylsulfoxide optimized at the MP2/6-31G* and B3-LYP/6-31G* (in square brackets) levels of theory.

nucleophile and modeling of solvation are needed to explain the experimental oxidation of thianthrene 5-oxide by dioxiranes.¹³

Because the gas phase reactivity of DMS and DMSO are comparable, the observed chemoselectivity for sulfide oxidation must be a consequence of solvent interactions in the condensed phase. The increase in dipole moment (Tables IS and IIS) in the transition state for oxygen atom transfer from DMDO to DMS (TS-3) is rather large because a highly polarized S—O bond is being formed. An increase in solvent polarity should stabilize the transition state (TS-3) for sulfide oxidation. Both the dipole moment and basicity of DMSO are greater than those of DMS.^{3a} Therefore, an increase in solvent polarity and the acidity of the solvent should stabilize the ground state of DMSO much more than its transition state for oxidation (TS-6). This is particularly true if a protic solvent is used. Indeed, the role of solvent polarity versus solvent acidity and the effects of such specific molecular interactions on the relative nucleophilicity of a sulfide versus a sulfoxide were clearly understood by Edwards and coworkers.¹⁹ These trends are now presented in a more quantitative way in Fig-

ure 4, where it is shown, based on a comparison with SCRF(PCM) calculations, that the solvated TS for sulfide oxidation is decreased from 27.3 to 13.4 kcal/mol (MP2/6-31G*) upon going from the gas to the condensed phase. Because of the greater stabilization of the ground state ($\Delta E_{\text{stab}} = -13.0$ kcal/mol), the activation energy for sulfone formation in the condensed phase decreases by only 0.5 kcal/mol with respect to that in the gas phase (Table I). Another factor that could conspire to lower the activation energy for sulfoxide oxidation is its relatively high exothermicity for sulfone formation (Table III).

Experimental studies on thianthrene 5-oxide indicate that oxidation by dioxiranes occurs more rapidly at the sulfide than the sulfoxide.¹³ By contrast, the QCISD(T) and B3-LYP calculations indicate the barrier for oxidation of H₂S is ca. 10 kcal/mol higher than H₂SO (Table I). This is primarily because H₂S and H₂SO are rather poor models for thianthrene 5-oxide. Dimethylsulfide and sulfoxide are better models, and the barrier for dimethyldioxirane oxidation of Me₂S is only 0.4–3 kcal/mol higher than that for Me₂SO.

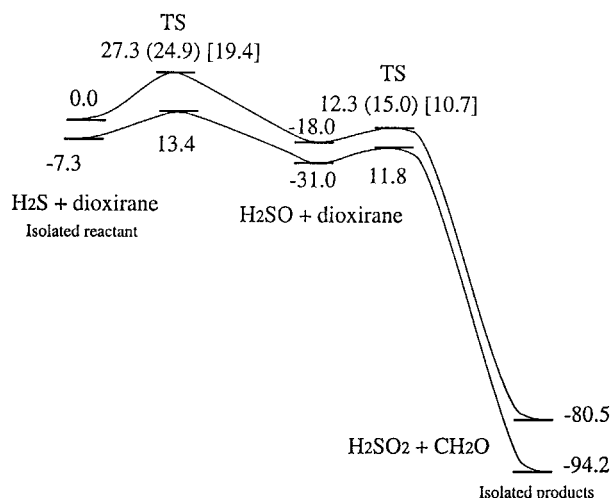


FIGURE 4. The relative energies and barrier heights (kcal/mol) for the oxidation of H_2S and H_2SO by the parent dioxirane at the MP2/6-31G*, QCISD(T)/6-31G*//MP2/6-31G* level (in parentheses), and B3-LYP/6-31G* level (in square brackets). The lower curve was calculated at the MP2/6-31G* level using Tomasi's PCM approach to model solvation in chloroform.

OXIDATION OF AMINES AND PHOSPHINES

We now extend these studies to include the oxidation of amines and phosphines by dioxiranes to provide a comparison with comparable oxygen atom transfer from peroxyformic acid.^{3a} The transition structures for the oxidation of NH_3 with dioxirane and dimethyldioxirane and NMe_3 with dimethyldioxirane are shown in Figure 5. The corresponding phosphine transition structures are given in Figure 6. For the amines, the attack is along the axis of the nitrogen lone pair; the N—H or N—C bonds in TS-8 and 9 are approximately equal and the N—O—O bond angle is slightly bent (Fig. 5). By contrast, attack of DMDO on phosphine occurs not on the lone pair, but anti to a P—H or P—C bond (Fig. 6; TS-11 and 12). This results in an elongation of the axial bond and yields a trigonal bipyramidal structure with an axial P—O bond and an equatorial lone pair. Analogous transition structures are found for the oxidation of amines and phosphines by peroxyformic acid^{3a} and carbonyl oxide (see subsequent text).

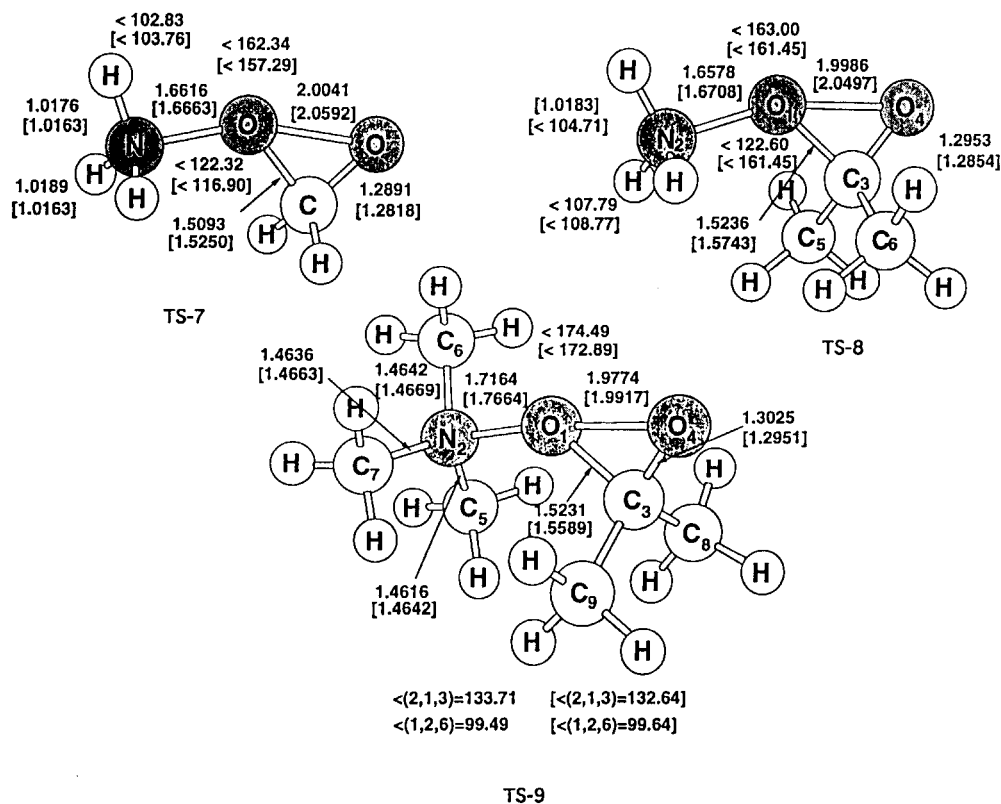


FIGURE 5. Transition structures for oxygen transfer from dioxirane and dimethyldioxirane to ammonia and trimethylamine optimized at the MP2/6-31G* and B3-LYP/6-31G* (in square brackets) levels of theory.

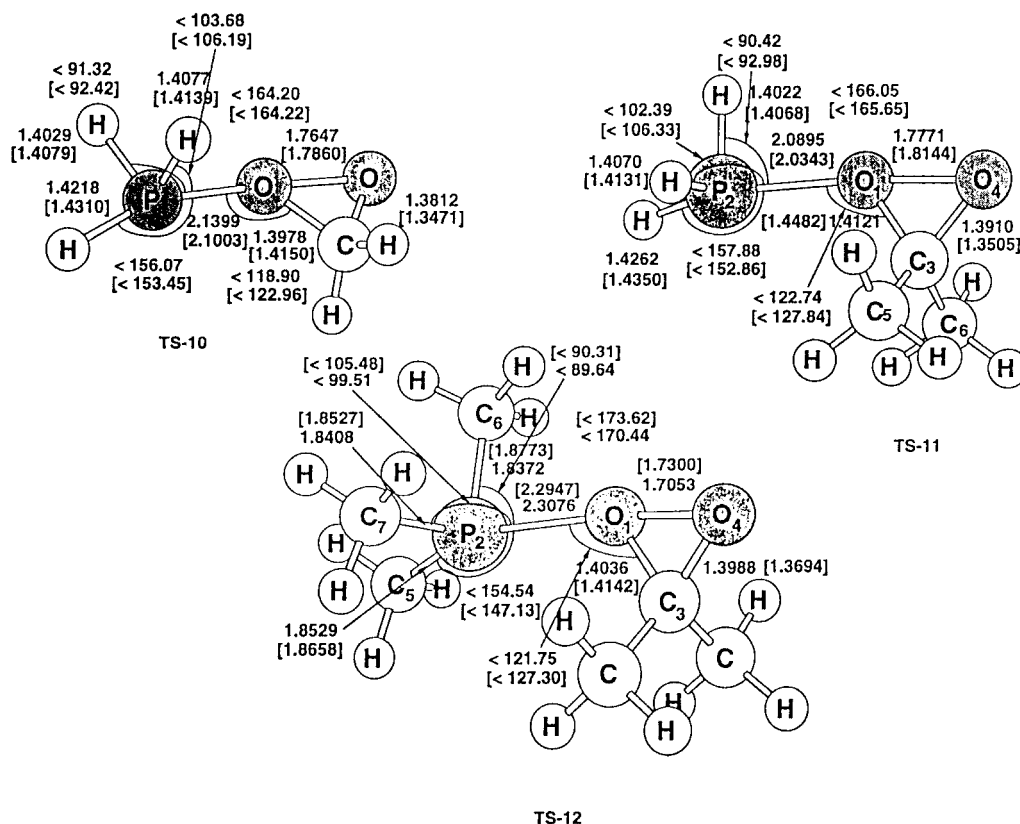


FIGURE 6. Transition structures for oxygen transfer from dioxirane and dimethyldioxirane to phosphine and trimethylphosphine optimized at the MP2/6-31G* and B3-LYP/6-31G* (in square brackets) levels of theory.

The gas phase barriers for NH_3 oxidation by dioxirane are 10–20 kcal/mol higher than for PH_3 . The MP4 and QCI calculations are in good agreement with each other for NH_3 , but do not agree as well for the reaction of PH_3 with DMDO because of the RHF \rightarrow UHF instability problems [however, recalculation at the UQCISD(T) level raises the barrier by only 4.0 kcal/mol].

The generally accepted reactivity trends for amines and phosphines are that the former are considered to be more basic, whereas the better nucleophilicity of the latter has been attributed to the greater polarizability of phosphorous. Our calculations^{3a} on the peroxyacid oxidation of NH_3 and PH_3 were indeed consistent with this conventional wisdom. However, because the intrinsic gas phase reactivity of methyl-substituted amines and phosphines are comparable,^{3a} we suggest that the observed reactivity trends are largely due to the greater solvation of the ground state tertiary amine. The classical activation barriers for the formation of $\text{H}_3\text{P}-\text{O}$ are lower than those for $\text{H}_3\text{N}-\text{O}$ formation when computed from the isolated reactants. However, when an SCRF correction is made

employing the Tomasi method,^{16a,b} the relative reactivity based on activation barriers for NH_3 and PH_3 oxidations is virtually identical.^{3a} Figure 7 summarizes the relative energies and barrier heights calculated for NH_3 and PH_3 oxidations with dioxirane at various levels of theory. The calculated solvation effects are larger for the amines than the phosphines, and the barrier heights are predicted to be quite close in the condensed phase.

Methyl substitution on dioxirane raises the barriers by 2–4 kcal/mol. Like the sulfides and sulfide oxidations, methyl substitution of the nucleophile lowers the barrier drastically. This is apparently caused by the higher exothermicity of the oxidation of methyl-substituted sulfides, amines, and phosphines with respect to their parent prototypes (see the B3-LYP values in Table III) that have later transition structures and, as a consequence, higher barriers (Tables I and II). The B3-LYP calculations correctly reproduce the trends, but the barriers are up to 7 kcal/mol lower than the QCISD(T) barriers. Similar underestimates of barriers calculated at the B3-LYP level were found for alkene

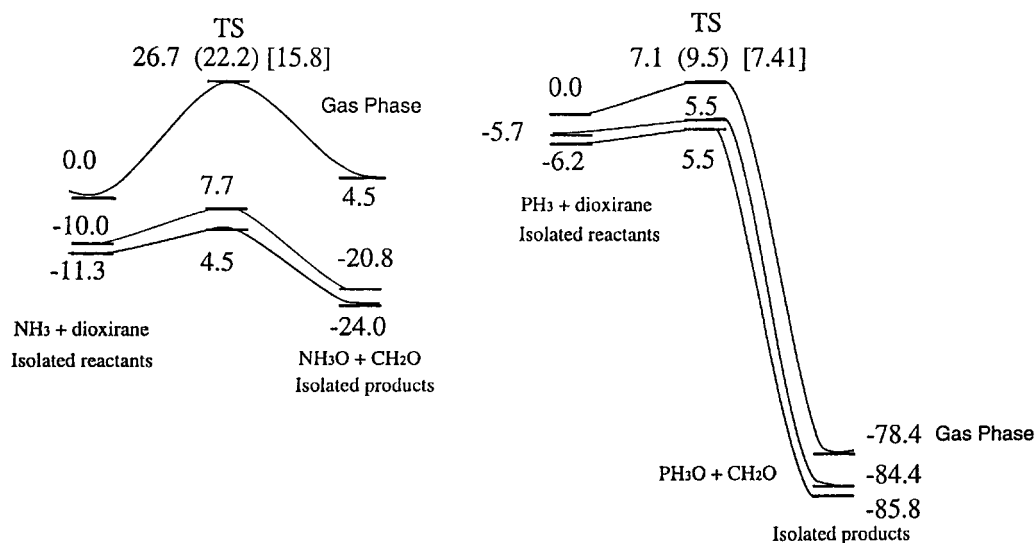


FIGURE 7. The relative energies and barrier heights (kcal/mol) for the oxidation of NH_3 and PH_3 by the parent dioxirane at the MP2/6-31G*, QCISD(T)/6-31G*//MP2/6-31G* level (in parentheses), and the B3-LYP/6-31G* level (in square brackets). The lower curves were calculated at the MP2/6-31G* level using Tomasi's PCM approach to model solvation in chloroform (middle curve) and methanol (bottom).

epoxidations with peroxyformic acid^{3d} and for $\text{S}_\text{N}2$ reactions at saturated carbon.²¹

As seen from Figure 8, the calculated barriers for the oxidations with peroxyformic acid^{3a} are lower than those for the oxidations of the same substrates with DMDO. The barriers are close for the oxidation of phosphine and trimethylphosphine. The barriers calculated at the B3-LYP/6-31G* level display a similar trend, although their values differ considerably from the MP4//MP2/6-31G* barriers for sulfides and amines (Table I).

CARBONYLOXIDE OXIDATION OF H_2S , H_2SO , NH_3 , PH_3 , AND ETHENE

We elected to include ethene in this series of nucleophiles because the carbon-carbon double bond is weakly nucleophilic and considerable experimental data on the formation of epoxides from alkenes is available.²² The transition states for oxidation by carbonyl oxide and dimethylcarbonyl oxide are shown in Figures 9 and 10, respectively. The orientation of attack is similar to that in the oxidation by dioxirane and by peroxyformic acid.^{3a} However, the X—O bonds are considerably longer, indicating a more reactant-like transition structure. This is in agreement with Hammond's postulate, because oxidation by carbonyl oxide is 20–30

kcal/mol more exothermic than oxidation by dioxirane, reflecting the higher ground state energy of carbonyl oxide (Table IV). In turn, reaction with unsubstituted carbonyl oxide is ca. 5 kcal/mol more exothermic than with dimethylcarbonyl oxide, with an even earlier transition state (Table III).

As a result of the greater exothermicity of the reactions with carbonyl oxide, the barriers are as much as to 10 kcal/mol lower than for oxidation by dioxirane (Table II). In contrast to dioxirane oxidation, the transition states for carbonyl oxide oxidation are not affected by the RHF \rightarrow UHF instability problems, and there is good agreement between the MP2, MP4, and QCISD(T) barrier heights. Methyl substitution on carbonyl oxide has very little effect on the barrier heights, but it can be anticipated that methyl substitution of the nucleophile would lower the barriers significantly. The calculated changes in the barriers due to solvation are much smaller than for dioxirane oxidation, primarily because the differences between the reactant and transition state dipoles are small (Tables II and IS).

The transition structures for the oxidation of alkenes with dioxirane and dimethyldioxirane are unsymmetrical at the MP2/6-31G* level, but the approach to the double bond is symmetrical at the QCISD/6-31G* and B3LYP/6-31G* levels.^{3d} The transition states for oxidation of ethene by car-

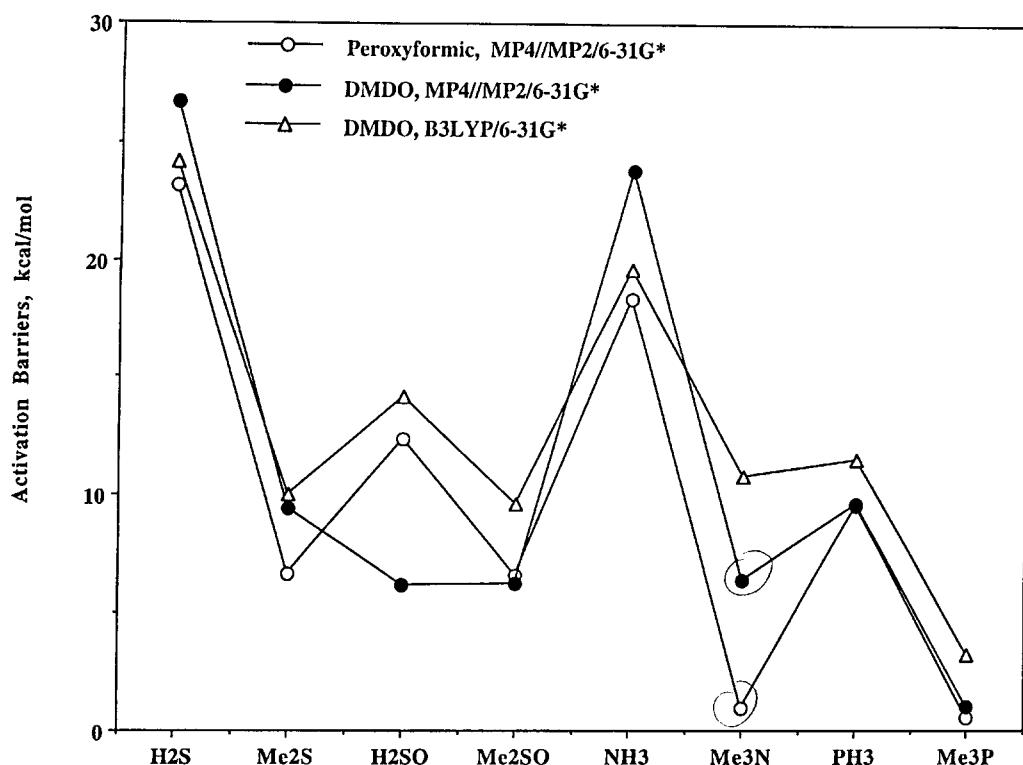


FIGURE 8. Trends in the activation barriers for oxidations with peroxyformic acid and DMDO calculated at the MP4/6-31G*//MP2/6-31G* and B3LYP/6-31G* levels.

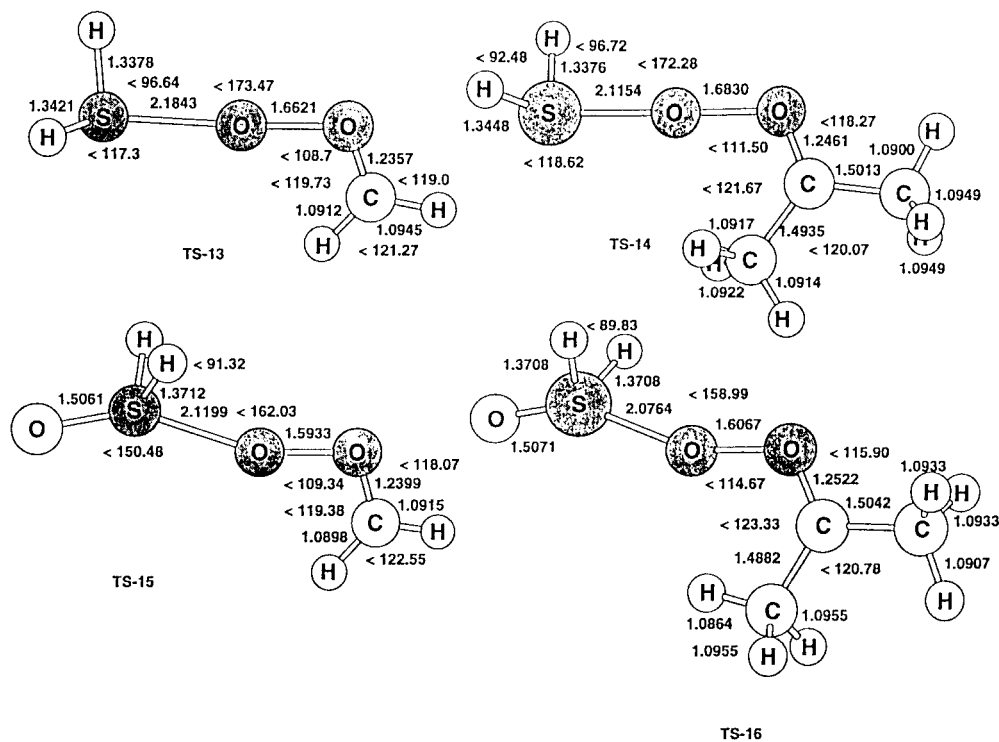


FIGURE 9. Transition structures for oxygen transfer from carbonyl oxide and dimethylcarbonyl oxide to hydrogen sulfide and dihydrogen sulfoxide optimized at the MP2/6-31G* level.

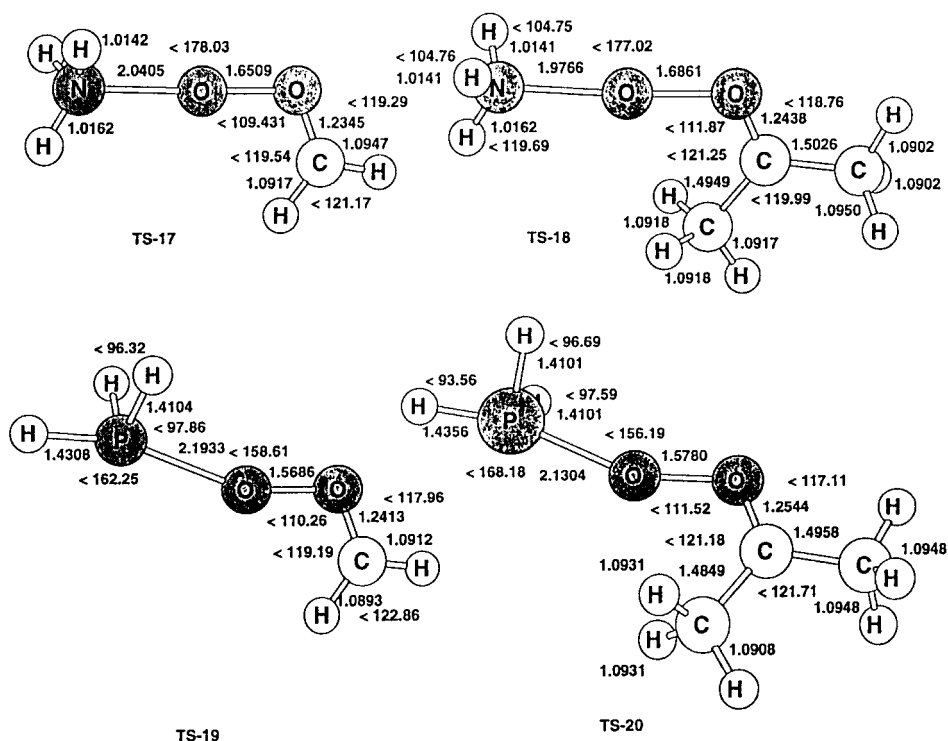


FIGURE 10. Transition structures for oxygen transfer from carbonyl oxide and dimethylcarbonyl oxide to ammonia and phosphine optimized at the MP2/6-31G* level of theory.

bonyloxides do not suffer from the same difficulties as those for dioxirane and peroxyformic acid. Even at the MP2/6-31G* level, the distances from the spiro oxygen to the carbon atoms are nearly identical (Fig. 11). The barriers at the MP2 and MP4 levels are similar and solvent has relatively

little effect on the barrier heights (Table II), and the calculated barriers agree well with experiment.¹² In a similar fashion, the oxidation of ethene by peroxyformic acid has been studied at the MP2/6-31G*, MP4/6-31G*, QCISD/6-31G*, CCSD(T)/6-31G*, and B3-LYP levels of theory.^{3d} The MP2/6-31G* calculations lead to an unsymmetrical transition structure for peroxy acid epoxidation that is an artifact of the level of theory. However, the QCISD/6-31G* and B3-LYP/6-31G* calculations both result in a symmetrical transition structure with essentially equal C—O bonds.

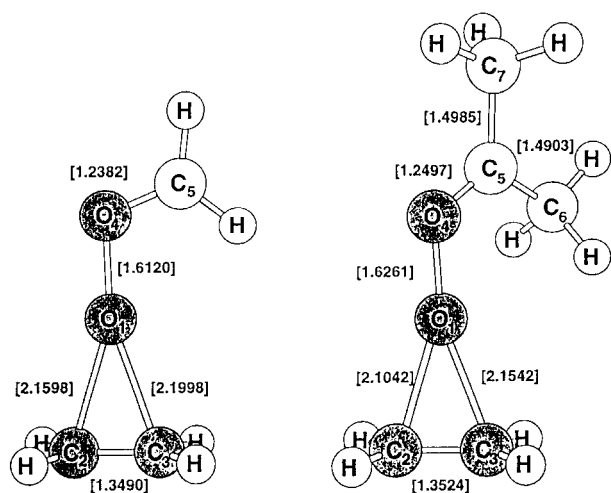


FIGURE 11. Transition structures for the epoxidation of ethene by carbonyl oxide and dimethylcarbonyl oxide calculated at MP2/6-31G* level of theory.

Conclusions

1. The barriers for oxygen transfer from dimethyldioxirane are higher (up to 2.5 kcal/mol for the oxidation of H₂S) than those for the oxidations with the parent dioxirane. The oxidation barriers for dioxirane are larger than those for the oxidations with peroxyformic acid, except for the barriers for oxidation of sulfoxides. The reactivity of dimethylsulfide toward dimethyldioxirane was found to be comparable to that of dimethylsulfoxide both in the gas phase and in solution (chloroform).

- The classical gas phase barrier for the oxidation of trimethylamine to trimethylamine oxide was higher (6.3 kcal/mol at the MP4//MP2/6-31G* level) than that for oxygen atom transfer to trimethylphosphine. When the transition structures were examined by self-consistent reaction field (SCRF) methods the predicted barriers for the oxidation of amines and phosphines were found to be in good agreement with experiment.
- The general trend in reactivity for oxidation by dioxirane is $R_2S \leq R_2SO$, $R_3P > R_3N$ in the gas phase, and $R_2S \leq R_2SO$, $R_3N \leq R_3P$ ($R = Me$) in solution.
- The oxidation barriers calculated using the B3-LYP functional are lower than those computed at the MP4 and QCISD(T) levels.
- The MP2/6-31G* level of theory yields good transition state geometries for the gas phase oxidation of the studied nucleophiles by carbonyloxides, but is not sufficient to produce barrier heights in accord with experiments. The problems with the barrier heights are due in part to the instability of the RHF wave functions, particularly for transition structures with long O—O distances. Calculations at the QCISD(T) level are affected less than at MP2 by problems of RHF \rightarrow UHF instability and spin contamination, and thus are better for computing barrier heights. The QCISD(T)/6-31G*//MP2/6-31G* level reduces the difference in barrier heights for oxidation of unsubstituted sulfides and unsubstituted sulfoxides.
- Oxidation of the nucleophiles examined including ethene by carbonyloxides gives results comparable with experiments, even at the MP2/6-31G* level, because the RHF wave functions are stable in all cases.
- The MP2 level of theory does not provide adequate geometries for the epoxidation of alkenes. We suggest that geometries be optimized at the B3-LYP level with energy refinement at the QCISD(T) or CCSD(T) levels.
- Methyl substituents on the nucleophiles lower the activation barriers considerably, whereas hydrogen substituents do not serve well as models for nucleophiles.

Acknowledgments

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